

U.S. Application No.: 10/588,597  
Office Action Mailed: March 9, 2010  
Amendment and Response filed May 31, 2010

### **REMARKS**

A final Office Action was mailed in the above-referenced matter on March 9, 2010. Claims 3, 5-10, and 19-31 were pending in the Application. Claims 3, 5-10, and 19-31 were rejected. Claims 21 and 22 have been amended to further clarify the specifics of the fixation method of the fixation step. Support for this amendment can be found in Example 1 and in Example 2 in the specification. It is believed that none of these amendments constitute new matter.

### **Withdrawn Rejections Under 35 U.S.C § 112-indefiniteness**

The Examiner has withdrawn the previous rejection under 35 U.S.C. 112, second paragraph, in view of the Applicant's previous remarks and amendments.

The Examiner has withdrawn the previous rejection under 35 U.S.C. § 102(b) as being anticipated by Hu (U.S. Patent No. 5,939,251) in view of the previous amendments.

### **Rejection Under 35 U.S.C. § 103(a) Nuovo et al., in view of Hu**

The Examiner has maintained the rejection of Claims 21 and 22 under 35 U.S.C. § 103(a) as being unpatentable over Nuovo et al., (*Genome Res.* 1993 2:305-312) in view of Hu (US Patent 5,939,251) and has now included Claims 3, 9, 10, 19, 23 and 28-30 in the rejection. The Office action reasons that the claimed invention “. . . requires that amplified nucleic acid exist in the PCR solution outside the cell. . .” and that “[w]ith regard to the newly amended claim requiring “dry fixation” (teaches fixation in 95% ethanol), “pre-treating” and “performing” steps, Nuovo teaches performing *in situ* PCR”. The teachings of Hu have been outlined previously in the non-final Office action dated August 28, 2009. The present Office action concludes that it would have been *prima facie* obvious to utilize the products and methods of Hu to perform the *in situ* PCR methods of Nuovo et al. since the prior art expressly recognizes that such PCRs could be performed more efficiently within such products. The Office action does note that Nuovo et al. does not expressly teach divided compartments of a support.

U.S. Application No.: 10/588,597  
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A *prima facie* case of obviousness has three distinct requirements. First, the references must teach or suggest every claim element. M.P.E.P. §§ 2142 and 2143.03. Second, there must be a motivation to modify or combine the teachings of the cited references. M.P.E.P. §§ 2143 and 2143.01. Third, there must be a reasonable expectation of success in performing the modified or combined teachings of the references. M.P.E.P. § 2143.02.

Applicants have amended Claims 21 and 22 to include the specifics of the fixation method in the “fixing” step. As noted in the Office action on pages 5 and 6, “. . . the inventive concept of the claimed invention is the fixation of cells such that the cellular wall allows for passage of nucleic acid to a level past that commonly accepted for *in situ* PCR i.e. dry fixed cells out to a point where large amounts of nucleic acid leak from them” and that “[s]uch a concept, i.e. promoting leakage of nucleic acid from fixed cells for amplification purposes, has not been found in the prior art”.

In view of the claim amendments, Applicants contend that neither Nuovo et al. nor Hu, either alone or in combination, teach or suggest the detection method as claimed and that since neither of these references alone or in combination teach each and every element of Claims 21 or 22 (nor the claims that depend from Claims 21 or 22) as amended, Applicants submit that Claims 3, 9, 10, 19, 21-23 and 28-30 are patentable over the cited references. The Applicants respectfully request that the rejection under 35 U.S.C 103 be withdrawn.

**Rejection Under 35 U.S.C. § 103(a) Nuovo et al. in view of Hu and further in view of Villeponteau et al.**

The Examiner has rejected Claims 5, 20, 24 and 31 under 35 U.S.C. § 103(a) as being unpatentable over Nuovo et al., (*Genome Res.* 1993 2:305-312), in view of Hu (U.S. Patent No. 5,939,251) as applied to Claims 21 and 22 above and further in view of Villeponteau et al., (U.S. Patent No. 5,776,679). The Office action asserts that the teachings of Nuovo et al. and Hu do not expressly teach the labeling of nucleic acids during PCR or detection of PCR products through electrophoresis but that Villeponteau et al. provides supportive disclosure that teaches labeling nucleic acids during *in situ* PCR through the incorporation of labeled nucleotides. Thus the

U.S. Application No.: 10/588,597  
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Office action asserts that it would have been *prima facie* obvious to one of skill to incorporate labeled nucleotides into the *in situ* PCR of Hu since the prior art expressly suggests such a modification to prevent leakage of PCR products and further that Villeponteau et al. teaches the detection of PCR products through electrophoresis.

Applicants have amended Claims 21 and 22 as described above. The teachings of Villeponteau et al. do not make up for the deficiencies of Nuovo et al. and Hu as described above. Applicants contend that in view of these amendments, that Claims 5, 20, 24 and 31, which are dependent upon amended Claims 21 or 22, are patentable over the cited references and respectfully requests that the rejection under 35 U.S.C § 103 be withdrawn.

**Rejection Under 35 U.S.C. § 103(a) Nuovo et al. in view of Hu in view of Villeponteau et al. and in further view of Stapleton et al.**

The Examiner has rejected Claims 6-8 and 25-27 under 35 U.S.C. § 103(a) as being unpatentable over Nuovo et al., (*Genome Res.* 1993 2:305-312), in view of Hu (U.S. Patent No. 5,939,251) in view of Villeponteau et al. (U.S. Patent No. 5,776,679) as applied to Claims 5 and 24 and in further view of Stapleton et al. (U.S. Patent No. 6,103,192). The Office action asserts that neither Nuovo et al., Hu, nor Villeponteau et al. expressly teach the detection of labeled PCR products through hybridization to immobilized probes in microarray format but that Stapleton et al. provides a supportive disclosure that teaches a method wherein various biological specimens are collected, dried, transported, stored and processed on matrices which adhere cells and viruses and that in summary it would have been *prima facie* obvious to a skilled person to detect the PCR products of Hu through use of immobilized probes in a microarray format since the prior art expressly suggested such a modification to allow for the analysis of multiple sequences at once.

Applicants have amended Claims 21 and 22 as described above. The teachings of Villeponteau et al. and Stapleton et al. do not make up for the deficiencies of Nuovo et al. and Hu as described above. Therefore, Applicants contend that in view of these amendments, that Claims 6-8 and 25-27, which are dependent on amended Claims 21 or 22, are patentable over the cited references and respectfully requests that the rejection under 35 U.S.C § 103 be withdrawn.

U.S. Application No.: 10/588,597  
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Closing Remarks

Applicant believes that the pending claims are in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-1970, if not otherwise specifically requested. The undersigned hereby authorizes the charge of any fees created by the filing of this document or any deficiency of fees submitted herewith to be charged to deposit account No. 19-1970.

Respectfully submitted,

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Date: May 31, 2010